In The Claims

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) An *in vitro* method for ~~inducing a conformational transition in recombinant proteins and/or variants thereof, whereas said conformational transition results in an increased~~ increasing the content of β-sheet secondary structure in recombinant amyloidogenic protiens, ~~the method~~ comprising ~~the steps of~~:

~~a) providing a conversion buffer;~~

~~b) adding a solution of lamellar lipid structures that comprise negatively charged lipids to the conversion buffer;~~

~~c) adding recombinant protein molecules and/or variants thereof to the conversion buffer;~~

~~d) forming a sample mixture from the conversion buffer, the added lipids and protein molecules;~~

~~e) establishing a conversion temperature in the sample mixture; and~~

~~f) exposing the sample mixture of step d) to the conversion temperature according to step e) for a time sufficient to form conformationally transitioned proteins;~~

a) mixing: a conversion buffer, a solution of lamellar lipid structures comprising negatively charged lipids, and recombinant amyloidogenic proteins to form a mixture at a temperature; and

b) exposing the mixture of step a) to a conversion temperature for a time sufficient to increase the β-sheet secondary structure in the recombinant amyloidgenic proteins;

wherein water soluble complexes of lamellar lipid ~~lipidic~~ structures and conformationally transitioned proteins are formed, the conformationally transitioned proteins being amyloidogenic oligomeric β-sheet intermediate structures.

2. (Currently Amended) ~~Method~~ The method according to claim 1, wherein amyloidogenic aggregates are produced [[of]] from the water soluble complexes of lamellar lipid ~~lipidic~~ structures and oligomeric β-sheet intermediate structures by actively destroying the lamellar lipid structures.

3. (Currently Amended) ~~Method~~ The method according to claim 2, wherein [[for]] producing said amyloidogenic aggregates comprises[[,]] destruction of the lamellar lipid structures of the water soluble complexes [[are]] ~~destroyed~~ by:

a) dilution of the solution of the water soluble complexes of lamellar lipid ~~lipidic~~ structures and oligomeric intermediate structures significantly below ~~the~~ critical micelle concentration of the lipids used; or

b) dilution of the solution of the water soluble complexes of lamellar lipid ~~lipidic~~ structures and oligomeric intermediate structures significantly below ~~the~~ critical micelle concentration of the lipids used and treatment of the so produced amyloidogenic aggregates with non-denaturing detergents ~~such as octylglucoside~~; or

c) directly treating the water soluble complexes of

lamellar lipid ~~lipidic~~ structures and oligomeric intermediate structures with detergent, without previous dilution of the lipids.

4. (Currently Amended) Method according to claim 1, wherein the solution of lamellar lipid structures in step [[b)]] a) is a bicellar lipid solution, the conversion temperature in step b) is higher than the temperature in step a), and the water solubule amyloidogenic ~~; in step c) the sample mixture is heated to a conversion temperature which is higher than the temperature for forming the sample mixture, and the water soluble~~ oligomeric β-sheet intermediate structure is an oligomeric β-sheet intermediate (PrP^{β}) which is aggregated into amyloid fibrils ($PrP^{\beta f}$).

5. (Currently Amended) ~~Method~~ The method according to claim 4, wherein the ~~sample mixture is heated in step c) to a~~ conversion temperature in step b) is in the range ~~from~~ of 37 °C to 65 °C.

6. (Currently Amended) ~~Method~~ The method according to claim 4, wherein ~~these~~ the amyloidogenic proteins are involved in[[:]]

[[a)]] neurodegenerative diseases ~~of the group comprising~~ selected from the group consisting of Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease[[;]] and~~/or~~ other [[b)]] conformational diseases ~~of the group comprising~~ selected from the group consisting of Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis.

7. (Original) The method of claim 1, wherein the conversion buffer comprises 25 mM long-chain (DMPX) and 25 mM short-chain (DHPC) phospholipids to form a bicellar solution.

8. (Currently Amended) The method of claim 7, wherein the long-chain phospholipid in the conversion buffer is ~~23,75~~ 23.75 mM (DMPC) and ~~1,25~~ 1.25 mM (DMPS or DMPG), and wherein the short-chain phospholipid is 25 mM (DHPC).

9. (Currently Amended) The method of claim 1, wherein the pH of the conversion buffer is below the isoelectric point of the recombinant amyloidogenic proteins.

10. (Original) Oligomeric β-sheet intermediate structures produced by an in vitro method for inducing a conformational transition in recombinant proteins and/or variants thereof, whereas said conformational transition results in an increased content of β-sheet secondary structure, the method comprising the steps of:

a) providing a conversion buffer;

c) adding a solution of lamellar lipid structures that comprise negatively charged lipids to the conversion buffer;

c) adding recombinant protein molecules and/or variants thereof to the conversion buffer;

d) forming a sample mixture from the conversion buffer, the added lipids and protein molecules;

e) establishing a conversion temperature in the sample mixture; and

f) exposing the sample mixture of step d) to the

conversion temperature according to step e) for a time sufficient to form conformationally transitioned proteins; wherein the oligomeric β-sheet intermediate structures are conformationally transitioned proteins that are part of water soluble complexes comprising lamellar lipidic structures.

11. (Original) Amyloidogenic aggregates produced from the oligomeric β-sheet intermediate structures of claim 10, wherein the amyloidogenic aggregates are derived of the oligomeric β-sheet intermediate structures by actively destroying the lamellar lipid structures of the water soluble complexes of lamellar lipidic structures and conformationally transitioned proteins.

12. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of amyloidogenic aggregates according to claim 11, for exploiting the various aspects of the conversion under controlled conditions.

13. (Original) Use of the method according to claim 6, for the screening for "conversion inhibitors" for the development of diagnostics and/or prophylactics and/or therapeutics against conformational diseases in humans and/or animals.

14. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of

amyloidogenic aggregates according to claim 11, for the screening for "conversion inhibitors" for the development of diagnostics and/or prophylactics and/or therapeutics against conformational diseases in humans and/or animals.

15. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of amyloidogenic aggregates according to claim 11, for the screening for ligands for the development of

a) therapeutics against conformational diseases in humans and/or animals; or

b) prophylactics against conformational diseases in humans and/or animals; or

c) diagnostic tests for conformational diseases in humans and/or animals.

16. (Original) Use of the method according to claim 6, for the screening for ligands for the development of

a) therapeutics against conformational diseases in humans and/or animals; or

c) prophylactics against conformational diseases in humans and/or animals; or

c) diagnostic tests for conformational diseases in humans and/or animals.

17. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of amyloidogenic aggregates according to claim 11, for the development of antibodies specifically binding to

conformationally transitioned proteins.

18. (Original) Use of the method according to claim 6, for the development of antibodies specifically binding to conformationally transitioned proteins.

19. (Original) Use of the method according to claim 1, for the industrial production of recombinant conformationally transitioned proteins.

20. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of amyloidogenic aggregates according to claim 11, for the determination of the three-dimensional structure of conformationally transitioned proteins using NMR spectroscopy, X-ray, or electron microscopy as a basis for the design of ligands.

21. (Original) Use of the method according to claim 1, for the determination of the three-dimensional structure of oligomeric β-sheet intermediate structures of the conformationally transitioned proteins and/or amyloidogenic aggregates using NMR spectroscopy, X-ray, or electron microscopy as a basis for the design of ligands.

22. (Original) Use of ligands as derived according to claims 15, 16, 20 or 21, for diagnosis and/or prophylactics and/or therapeutic treatment of conformational diseases in humans and/or animals.

23. (Original) Use of "conversion inhibitors" as derived according to claims 13 or 14, for diagnosis and/or prophylactics and/or therapeutic treatment of conformational diseases in humans and/or animals.

24. (Original) Use of antibodies as derived according to claims 17 or 18, for diagnosis and/or prophylactics and/or therapeutic treatment of conformational diseases in humans and/or animals.

25. (Original) Use of the water soluble complexes of oligomeric β-sheet intermediate structures and lamellar lipidic structures according to claim 10 or of amyloidogenic aggregates according to claim 11, for the active immunization of humans or animals against neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis.

26. (Original) Use of antibodies as derived according to claims 17 or 18 for the manufacture of a medicament for passive immunisation of humans or animals against neurodegenerative diseases of the group comprising Transmissible Spongiform Encephalopathy (TSE), Alzheimers disease, Multiple Sclerosis, and Parkinsons disease; and/or other conformational diseases of the group comprising Primary systematic amyloidosis, Type II diabetes, and Atrial amyloidosis.

27. (Original) Composition for diagnosis or therapeutical or prophylactical treatment of human and/or animal conformational diseases, comprising "conversion inhibitors" as obtained according to the method of claim 13 or 14.

28. (Original) Composition for diagnosis or therapeutical or prophylactical treatment of human and/or animal conformational diseases, comprising ligands as obtained according to the method of claim 15, 16, 20 or 21.

29. (Original) Composition for diagnosis or therapeutical or prophylactical treatment of human and/or animal conformational diseases, comprising antibodies specifically binding to conformationally transitioned proteins as obtained according to the method of claim 17 or 18.